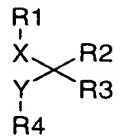
CLAIMS

1. A compound of general Formula I



(I)

or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R_1 represents,

C_1-C_6 alkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

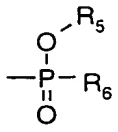
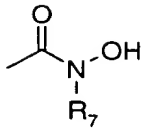
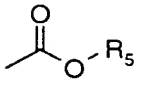
heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O, and substituted with one or more basic groups such as amino, amidino and/or guanidino;

or aryl, substituted with one or more basic groups such as amino, amidino and/or guanidino,

R_2 represents H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, Z_2N-CO-O-, ZO-CO-NZ- or Z_2N-CO-NZ- group,

R_3 represents $COOR_5$, $SO(OR_5)$, SO_3R_5, $P{=}O(OR_5)_2$, $B(OR_5)_2$, $P{=}OR_5(OR_5)$, or tetrazole, or any carboxylic acid isostere,

R_4 represents a  -group, or a  -group, or a  -group, roup,

R_5 represents H, C_1-C_6 alkyl or aryl,

R_6 represents C_1-C_6 alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted H_2N-C(Z)-CONH-C(Z)- or H_2N-C(Z)- group,

R_7 represents H or C_1-C_6 alkyl,

X represents O, S, SO, SO_2, $C(Z)_2$, N(Z), NR_7SO_2, SO_2NR_7, NR_7CO or $CONR_7$,

Y represents O, N(Z), S, $C(Z)_2$, or a single bond,

Z represents independently H, C_1-C_6 alkyl, aryl, cycloalkyl or heterocyclyl,

with the proviso that when X represents O, S, SO, SO_2, N(Z), NR_7SO_2, SO_2NR_7, or NR_7CO then Y represents $C(Z)_2$ or a single bond.

2. The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

R_1 represents,

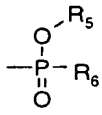
cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O, and substituted with one or more basic groups such as amino, amidino and/or guanidino;

R_2 represents H, C_1-C_3 alkyl, amino, halogen, hydroxy,

R_3 represents $COOR_5$,

R_4 represents a  -group,

R_5 represents H, C_1-C_6 alkyl or aryl,

R_6 represents C_1-C_6 alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted H_2N-C(Z)-CONH-C(Z)- or H_2N-C(Z)- group,

X represents $C(Z)_2$,

Y represents O or $C(Z)_2$,

Z represents independently H or C_1-C_6 alkyl.

3. The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

R_1 represents,

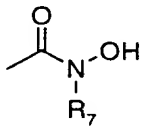
cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O, and substituted with one or more basic groups such as amino, amidino and/or guanidino;

R_2 represents H, C_1-C_3 alkyl, amino, halogen or hydroxy,

R_3 represents $COOR_5$,

R_4 represents a  -group,

R_5 represents H, C_1-C_6 alkyl or aryl,

R_7 represents H or C_1-C_6 alkyl,

X represents $C(Z)_2$,

Y represents $C(Z)_2$, or a single bond,

Z represents independently H or C_1-C_6 alkyl.

4. The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

R_1 represents,

cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

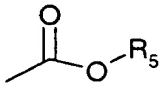
heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O,

and substituted with one or more basic groups such as amino, amidino and/or guanidino;

R_2 represents H, C_1-C_3 alkyl, amino, halogen or hydroxy,

R_3 represents $COOR_5$,

R_4 represents a  -group,

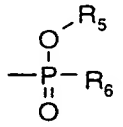
R_5 represents H, C_1-C_6 alkyl or aryl,

X represents $C(Z)_2$,

Y represents $C(Z)_2$, or a single bond,

Z represents independently H or C_1-C_6 alkyl.

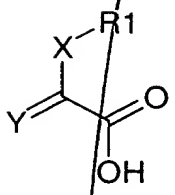
5. A process for the preparation of a compound according to any one of claims 1-4, wherein R_1, R_5, R_6, and Z are as defined in claim 1 and R_2 is H, R_3 is $COOR_5$,

R_4 represents a  -group,

X is $C(Z)_2$, Y is $C(Z)_2$,

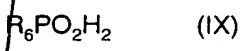
comprising the step of:

reacting a compound of Formula VI,



(VI)

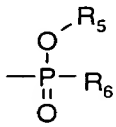
wherein R_1 and Z is as defined in claim 1 and X is $C(Z)_2$ and Y is $C(Z)_2$ with a compound of Formula IX,



(IX)

wherein R_6 is as defined in claim 1, in the presence of a suitable reagent, such as BSA or HMDS, under standard conditions.

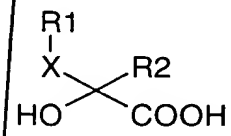
6. A process for the preparation of a compound according to any one of claims 1-4, wherein R_1, R_2, R_5, R_6, and Z are as defined in claim 1, R_3 is $COOR_5$, X is $C(Z)_2$, Y is O,

R_4 represents a  -group,

and

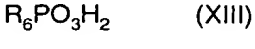
comprising the step of:

reacting a compound of Formula XII,



(XII)

wherein R_1 and R_2 are as defined in claim 1 and X is $C(Z)_2$ with a compound of Formula XIII,

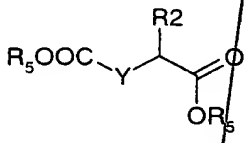


(XIII)

wherein R_6 is as defined in claim 1, in the presence of suitable coupling reagents such a DCC/DMAP, PyBop/DIPEA or $SOCl_2$, under standard conditions.

7. A process for the preparation of a compound according to any one of claims 1-4, wherein R_1 and R_2 are as defined in claim 1 and X and Y is $C(Z)_2$ or a single bond and R_3 and R_4 are $COOR_5$, comprising the step of:

reacting a compound of Formula XIV,



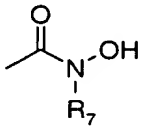
(XIV)

wherein R_2 and R_5 are as defined in claim 1 and Y is $C(Z)_2$ or a single bond, with a compound of the general Formula III,

(III)

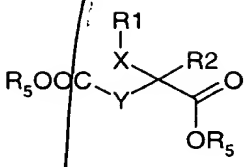
wherein R_1 is as defined in claim 1, X is $C(Z)_2$ and L is a suitable leaving group, such as Cl, Br, I or tosyl, in the presence of a suitable base, such as LDA or NaH, under standard conditions.

8. A process for the preparation of a compound according to any one of claims 1-4, wherein R_1, R_2, R_5, R_7, X, Y and Z are as defined in claim 1, R_3 is $COOR_5$ and

R_4 represents a  -group,

comprising the step of:

reacting a compound of Formula XV,



(XV)

with a compound of Formula XVI,

$$HR_7NOH \qquad \text{(XVI)}$$

wherein R_7 is as defined in claim 1, in the presence of suitable reagents, such as DCC/DMAP, under standard conditions.

9. A pharmaceutical formulation containing a compound according to any one of claims 1-4 as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

10. The use of a compound according to any one of claims 1 to 4 in therapy.

11. The use of a compound according to any one of claims 1 to 4 for the manufacture of a medicament for the inhibition of carboxypeptidase U.

12. A method for treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising administering to a mammal, including man, in need of such treatment an effective amount of a compound as defined in any of claims 1-4.

13. A pharmaceutical formulation for use in the treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising a compound as defined in any one of claims 1-4 in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

14. A pharmaceutical formulation, comprising:

(i) a compound of Formula I or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, and

(ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P_2T) antagonist,

in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

15. A kit of parts comprising:

(i) a pharmaceutical formulation containing a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and

(ii) a pharmaceutical formulation containing one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P_2T) antagonist, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier;

which compound (i) and agent (ii) are each provided in a form that is suitable for administration in conjunction with the other.

16. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a therapeutically effective total amount of

(i) a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; in conjunction with

(ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P_2T) antagonist,

in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

17. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a formulation as defined in claim 15.